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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/405,504	09/23/1999	ANDREAS STAHL	WHI9721P3MC2	9550

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EXAMINER

WEGERT, SANDRA L

ART UNIT	PAPER NUMBER
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1647

DATE MAILED: 03/27/2002

18

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/405,504

Applicant(s)

STAHL ET AL.

Examiner

Sandra Wegert

Art Unit

1647

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 07 January 2002.
- 2a) ☐ This action is FINAL. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 73, 74, 78 and 80-123 is/are pending in the application.

4a) Of the above claim(s) 98, 99, 102, 103, 105, 106, 108, 109, 112, 113, 115, 116 and 119-122 is/are withdrawn from consideration.

- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 73, 74, 78, 80-97, 100, 101, 104, 107, 110, 111, 114, 117, 118 is/are rejected.
- 7) ☒ Claim(s) _____ is/are objected to.
- 8) ☒ Claim(s) 73, 74, 78 and 80-123 are subject to restriction and/or election requirement.

Application Papers

- 9) ☒ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

DETAILED ACTION

Status of Application, Amendments, and/or Claims

The Information Disclosure Statement, filed 11/26/99, and the Supplemental Information Disclosure Statement, filed 3/23/00, have been entered into the record. Applicant's election of Group III, Claims 19, 23, 27, 29, 31, 33, 35, 55-57, 59, 67, 69, 71, 73-74, 78 and 80-81 in Paper 16 (1/7/02) is acknowledged. Likewise, Applicant elected SEQ ID NO: 24 for prosecution. Claims 1-72, 75-77 and 79 were cancelled by the Applicant in Paper 16; Claims 82-123 were added and read on the elected Invention. Applicant's election with traverse of SEQ ID NO: 24 is acknowledged. The traversal is on the grounds that SEQ ID NO's 24, 25 and 46 are related and encode FATP1 protein. The Examiner agrees that both SEQ ID NO's 24, and 46 both encode the polypeptide of SEQ ID NO: 25. In addition, since some of the claims read on generic methods for using the polynucleotides, it is appropriate to include the closely-related polynucleotides in the elected Invention.

Claims 73, 74, 78 and 80-123 and the nucleotides encoding SEQ ID NO: 24 are under examination in the instant application.

Informalities

Specification:

The specification is objected to for the following informalities:

URL's

The disclosure is objected to because it contains browser-executable code. This occurs, for example, on p. 33, line 6. All URL's should be removed from the Specification. Applicant may refer to web sites by non-executable name only (e.g., "The GAP program in the GCG software package"). See MPEP § 608.01 (p).

Appropriate correction is required.

Title

The title of the invention is not descriptive. A new title is required that is clearly indicative of the invention to which the claims are directed. The following title is suggested: "METHODS OF IDENTIFYING INHIBITORS OF FATTY ACID TRANSPORT PROTEIN FATP".

Appropriate correction is requested.

Claim Objections/Rejections

35 USC § 112, first paragraph-Scope of Enablement

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 73,74,78, 80-97, 100, 101, 104, 107, 110, 111, 114, 117 and 118 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of identifying *FATP* inhibitors for the transporter encoded by the polynucleotides of SEQ ID NO: 24 and 46, does not reasonably provide enablement for a method of identifying the ligands of *all FATP* transporters. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make the invention commensurate in scope with these claims.

The claims are directed to methods of determining whether a drug or substrate is an inhibitor of fatty acid transporter *FATP*, using cells transfected with an expression construct encoding a *FATP* transporter. The claims do not recite any structural limitation for the *FATP* transporter. The specification discloses a *FATP* protein having an amino acid sequence shown in SEQ ID NO: 25, as well as assays for identifying *FATP* ligands using cells recombinantly expressing SEQ ID NO: 25. The scope of the patent protection sought by the Applicant as defined by the claims fails to correlate reasonably with the scope of enabling disclosure set forth in the specification for the following reasons:

In In re Wands, 8USPQ2d, 1400 (CAFC 1988) page 1404, the factors to be considered in determining whether a disclosure would require undue experimentation include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6)

the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims.

Claims 73,74,78, 80-97, 100, 101, 104, 107, 110, 111, 114, 117 and 118 are rejected since they recite a "*FATPX*" transporter. However, the breadth of the claims is too extensive. Applicants are not enabled for *all FATP* transporters. Applicants are only enabled for the polynucleotides encoding the *FATP* transporter of SEQ ID NO 25. In addition, Applicants have not provided guidance or working examples with regard to how to make all possible *FATP* transporters, including ones that have yet to be discovered. Nor is it predictable to one of ordinary skill in the art how to make all *FATP* transporters besides those disclosed in the specification. A large quantity of experimentation is required to make all of the *FATP* transporters encompassed by the claims and evaluate them to see if they are useful in the claimed assays. Lastly, the nature of the invention is complex, especially given the intricacies and lack of predictability concerning interactions between complex biological molecules such as receptors and their specific binding partners. Substrate affinities for closely related transporters can differ dramatically. The nucleoside transporters *LdNTX* in *Leishmania* are examples in which experimenters have created fully-functional *new LdNTX* transporters with as few as two point mutations (2001, Vasudevan, et al, PNAS, 98: 6092).

Therefore, due to the large breadth of the claims regarding *all FATP* transporters, along with a lack of guidance and working examples of how to make and use all *FATP* transporters, as well as the unpredictability in the art of how to make said transporters, the Examiner believes that undue experimentation would be necessary to practice the method of using all *FATP*

transporters as claimed. This rejection can be overcome if Applicants amend the claims to recite specific Sequence ID Numbers.

Furthermore claims 104-106 and 114-116 are not enabled under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for use of the nucleic acid encoding the full length peptide, does not reasonably provide enablement for various protein forms of *FATP*, wherein the DNA sequence is at least 95% identical to the disclosed nucleic acid sequences. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make the invention commensurate in scope with these claims.

The claims are directed to use of a polynucleotide encoding a *FATP* transporter polypeptide to search for inhibitors of the transporter. The specification discloses a *FATP* transporter encoded by the DNA of SEQ ID NO: 24 and 46, having an amino acid sequence shown in SEQ ID NO: 25, as well as methods for recombinantly expressing SEQ ID NO: 25. The scope of the patent protection sought by the Applicant as defined by the claims fails to correlate reasonably with the scope of enabling disclosure set forth in the specification for the following reasons:

The specification discloses an enabled utility for the fatty acid transporter encoded by the DNA of SEQ ID NO: 24 and 46, as to be used to identify inhibitors of the transporter. However, there is no discussion, or working examples disclosed in the instant case, as to what amino acids are necessary to maintain the functional characteristics of the claimed polynucleotides encoding the *FATP* transporter polypeptide. The instant case claims altering as much as 5% of the

polynucleotide encoding the polypeptide of SEQ ID NO: 25. However, the art shows that receptor families have members with high structural similarities but disparate functions. For example, Smith et al. (1997, Nature Biotechnology 15:1222-1223) demonstrate that there are numerous cases in which proteins having very different functions share structural similarity due to evolution from a common ancestral gene. Brenner (1999, Trends in Genetics 15:132-133) argues that accurate inference of function from homology must be a difficult problem since, assuming there are only about 1000 major gene superfamilies in nature, then most homologs must have different molecular and cellular functions. Bisson, *et al* (1993, Crit Rev Biochem Mol Biol, 28:259) studied yeast transporter knockout phenotypes, and found little correlation between homology and the substrate transported. For example, they found that yeast transporters *Gal2* and *Hxt4* displayed 83.7% homology, but *Gal2* appears to transport Galactose, while *Hxt4* appears to transport Glucose (based on knockout phenotype- compare Table 1 and Table 2A). Similarly, Liang et al found that only a few amino acid substitutions in glucose transporters can change substrate specificity dramatically (1998, Liang, H., et al, Mol. Cell. Biol. 18(2): 926). Finally, Atsushi, et al (1996, J. Biol. Chem. 271: 30360) found that changing select amino acids in an acyl-CoA synthetase enzyme -less than 3% of the total residues- resulted in a functional fatty acid transporter (see Fig. 8).

In In re Wands, 8USPQ2d, 1400 (CAFC 1988) page 1404, the factors to be considered in determining whether a disclosure would require undue experimentation include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6)

the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims.

Due to the large quantity of experimentation required to determine how to use the variants of SEQ ID NO:25, the lack of direction or guidance in the specification regarding same (e.g., what amino acids are necessary to maintain the functional characteristics of the polypeptide encoded by the claimed polynucleotide of SEQ ID NO: 24 and 46), the lack of working examples to variants of SEQ ID NO: 25, the state of the art showing the unpredictability of function based on structural similarity of receptor proteins, and the breadth of the claims which embrace innumerable variants of SEQ ID NO: 25, undue experimentation would be required of the skilled artisan to make and use the claimed invention in its full scope.

Conclusion:

Claims 73,74,78, 80-97, 100, 101, 104, 107, 110, 111, 114, 117 and 118 are rejected for the reasons cited above.

Advisory Information

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sandra Wegert whose telephone number is (703) 308-9346. The examiner can normally be reached Monday - Friday from 9:00 AM to 5:00 PM (Eastern Time). If attempts to reach the examiner by telephone are unsuccessful, the Examiner's supervisor, Gary Kunz, can be reached at (703) 308-4623.

Official papers filed by fax should be directed to (703) 308-4242. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

SLW

3/18/02

Elizabeth C. Kemmerer

**ELIZABETH KEMMERER
PRIMARY EXAMINER**